

**Amendments to the Specification:**

Please replace paragraph [0022] beginning at page 5, line 17, with the following:

--[0022]        Figures 2a-2d show the sequence comparison of human hexokinase V (SEQ ID NO:2) to other hexokinases (SEQ ID NOS:5-8).--

Please replace paragraph [0095] beginning at page 25, line 15, with the following:

--[0095]        Immunoaffinity chromatography using antibodies raised to a variety of affinity tags such as hemagglutinin (HA), FLAG, Xpress, Myc, hexahistidine (SEQ ID NO:9) (His), glutathione S transferase (GST) and the like can be used to purify polypeptides. The His tag will also act as a chelating agent for certain metals (e.g., Ni) and thus the metals can also be used to purify His-containing polypeptides. After purification, the tag is optionally removed by specific proteolytic cleavage.--

Please replace paragraph [0175] beginning at page 46, line 3, with the following:

--[0175]        Common linkers such as peptides, polyethers, and the like can also serve as tags, and include polypeptide sequences, such as ~~poly-gly~~ poly-Gly sequences of between about 5 and 200 amino acids (SEQ ID NO:10). Such flexible linkers are known to those of skill in the art. For example, ~~poly(ethylene glycol)~~ poly(ethylene glycol) linkers are available from Shearwater Polymers, Inc., Huntsville, Alabama. These linkers optionally have amide linkages, sulfhydryl linkages, or heterofunctional linkages.--

Please replace paragraph [0222] beginning at page 59, line 1, with the following:

--[0222] RT-PCR was also used to survey tissues for the presence or absence of each of the mammalian hexokinases (Figure 4). Human pancreas, liver, kidney, brain, skeletal muscle and spleen cDNA were obtained from Ambion (PCR-ready cDNAs). Human islet cDNA were generated in house. For each member of the hexokinase family, gene-specific primers were designed based on the sequences. All reactions were run in parallel with GAPDH primers used as a positive control. Significant amounts of HKV mRNA were detected in human isolated pancreatic islets, human pancreas and human kidney. A faint signal was observed in human liver. Overall, these results show that HKV tissue distribution is more restricted than HKI, HKII or HKIII.

PCR primers for mammalian hexokinases tissue distribution:

HKI forward	5' GCTGGAGATGGAAAATCACACCACC 3' ( <u>SEQ ID NO:11</u> )
HKI reverse	5' CCCCCCACGAGACAAACAGAATG 3' ( <u>SEQ ID NO:12</u> )
HKII forward	5' GGGAAGGGGGAGTTTTTAGTTTGTTTTAC 3' ( <u>SEQ ID NO:13</u> )
HKII reverse	5' CCACAGGCGAATGAGGTATTTCTATGAC 3' ( <u>SEQ ID NO:14</u> )
HKIII forward	5'[[ - ]] TTGCGGCAGGGGGAAGAAAC [[ - ]]3' ( <u>SEQ ID NO:15</u> )
HKIII reverse	5'[[ - ]] CACCACGAAGTCTCCTTGCTCAGTG [[ - ]]3' ( <u>SEQ ID NO:16</u> )
HKIV forward	5' CTGAGTGGCTTGTGATTCTGGGATG 3' ( <u>SEQ ID NO:17</u> )
HKIV reverse	5' CTGCTTGGGGTTTCTTCCTGAGC 3' ( <u>SEQ ID NO:18</u> )
HKV forward	5' CTATGGCTTTCAGTCTTGTGGCTGC 3' ( <u>SEQ ID NO:19</u> )
HKV reverse	5' AGTGCTCCCTGGCAATCAACCTC 3' ( <u>SEQ ID NO:20</u> )
Human GAPDH forward	5'[[ - ]] GAGAAGGCTGGGGCTCATTTGC [[ - ]]3' ( <u>SEQ ID NO:21</u> )

Human GAPDH[[]] reverse 5'[[]] TGTCGCTGTTGAAGTCAGAGGAGACC [[]]3' (SEQ ID NO:22)--

Please replace paragraph [0227] beginning at page 60, line 29, with the following:

--[0227] The mRNA levels of mouse hexokinase V were quantified by real-time PCR using the SYBR® green I dye (SYBR® green RT-PCR reagents kit, Applied Biosystems, Foster City, CA). For each islet sample, 1 µg of total RNA was reverse transcribed to generate cDNA according to the manufacturer's instructions. The sequences of the gene-specific primers were as follow: mHK5: 5'- CTGCAGGAGACGGTGAAAGAG -3' (sense; SEQ ID NO:23) and 5'- CGCTGCCGTCTTCTGACA -3' (antisense; SEQ ID NO:24). Direct detection of PCR product was monitored by measuring the increase in fluorescence caused by the binding of SYBR® green dye to double stranded DNA with an ABI Prism 7700 sequence detection system (Applied Biosystems, Foster City, CA). Absence of non-specific or genomic amplification was assessed by including a non-template control and minus RT controls. The fluorescent signal in each sample was normalized to a corresponding β-actin signal (endogenous control) using the following mouse β-actin primers: 5'- CGTGAAAAGATGACCCAGATCA -3' (sense; SEQ ID NO:25) and 5'- CACAGCCTGGATGGCTACGT -3' (antisense; SEQ ID NO:26). Fold changes were calculated by using the comparative CT method. Results represent 2 (high fat fed) to 3 (db/db) individual islet preparations.--

Please replace paragraph (SEQ ID NO:1, Table of Sequences) beginning at page 63, line 2, with the following:

--SEQ ID NO:1 Human hexokinase V nucleic acid sequence (start methionine is underlined and indicated in bold; stop codon is underlined; Thymidine residue vs SEQ ID NO:3 variant is indicated in bold in large font)

ATGTTTGC GGTC CACTTGATGGCATT TTTACTTCAGCAAGCTGAAGGAGGACCAGATCAAGAAGGTGGA  
CAGGTTCTGTATCACATGCGGCTCTCCGATGACACCCTTTTGGACATCATGAGGCGGTTCCGGGCTG  
AGATGGAGAAGGGCCTGGCAAAGGACACCAACCCACGGCTGCAGTGAAGATGTTGCCACCTTCGTC  
AGGGCCATTCCCGATGGTTCCGAAAATGGGGAGTTCTTTCCCTGGATCTCGGAGGGTCCAAGTTCCG  
AGTGCTGAAGGTGCAAGTCGCTGAAGAGGGGAAGCGACACGTGCAGATGGAGAGTCAGTTCTACCCAA  
CGCCCAATGAAATCATCCGCGGGAACGGCATAGAGCTGTTTGAATATGTAGCTGACTGTCTGGCAGAT  
TTCATGAAGACCAAAGATT TAAAGCATAAGAAATTGCCCCCTTGGCCTAACTTTTTCTTTCCCCTGTCTG  
ACAGACTAAACTGGAAGAGGGTGTCTACTTTTCGTGGACAAAAAGTTTAAGGCACGAGGAGTTCAGG  
ACACGGATGTGGTGAGCCGTCTGACCAAAGCCATGAGAAGACACAAGGACATGGACGTGGACATCCTG  
GCCCTGGTCAATGACACCGTGGGGACCATGATGACCTGTGCCTATGACGACCCCTACTGCGAAGTTGG  
TGTCATCATCGGAAGTGGCACCAATGCGTGTTACATGGAGGACATGAGCAACATTGACCTGGTGGAGG  
GCGACGAGGGCAGGATGTGCATCAACACAGAGTGGGGGGCCTTCGGGGACGACGGGGCCCTGGAGGAC  
ATTGCACTGAGTTTCGACAGGGAGCTGGACCTCGGCTCTCTCAACCCAGGAAAGCAACTGTTTCGAGAA  
GATGATCAGTGGCCTGTACCTGGGGGAGCTTGTCTAGGCTTATCTTGCTGAAGATGGCCAAGGCTGGCC  
TCCTGTTTGGTGGTGAGAAATCTTCTGCTCTCCACACTAAGGGCAAGATCGAAACACGGCACGTGGCT  
GCCATGGAGAAGTATAAAGAAGGCCTTGCTAATACAAGAGAGATCCTGGTGGACCTGGGTCTGGAACC  
GTCTGAGGCTGACTGCATTGCCGTCCAGCATGTCTGTACCATCGTCTCCTTCGGCTCGGCCAATCTCT  
GTGCAGCAGCTCTGGCGGCCATCCTGACACGCCTCCGGGAGAAACAAGAAGGTGGAACGGCTCCGGACC  
ACAGTGGGCATGGACGGCACCCCTCTACAAGATAACCCCTCAGTACCCAAAACGCCTGCACAAGGTGGT  
GAGGAAACTGGTCCCAAGCTGTGATGTCCGCTTCCTCCTGTCAGAGAGTGGCAGCACCAAGGGGGCCC  
CCATGGTGACCGCGGTGGCCTCCCGCGTGCAGGCCAGCGGAAGCAGATCGACAGGGTGTCTGGCTTTG  
TTCCAGCTGACCCGAGAGCAGCTCGTGGACGTGCAGGCCAAGATGCGGGCTGAGCTGGAGTATGGGCT  
GAAGAAGAAGAGCCACGGGCTGGCCACGGTCAGGATGCTGCCCACCTACGTCTGCGGGCTGCCGGACG  
GCACAGAGAAAGGAAAGTTTCTCGCCCTGGATCTTGGGGGAACCAACTTCCGGGTCTCCTGGTGAAG  
ATCAGAAGTGGACGGAGGTCAGTGCGAATGTACAACAAGATCTTCGCCATCCCCCTGGAGATCATGCA  
GGGCACTGGTGAGGAGCTCTTTGATCACATTGTGCAGTGCATCGCCGACTTCCTGGACTACATGGGCC  
TCAAGGGAGCCTCCCTACCTTTGGGCTTCACATTCTCATTTCCCTGCAGGCAGATGAGCATTGACAAG  
GGAACACTCATAGGTGGACCAAGGTTTCAAGGCCACTGACTGTGAAGGGGAGGACGTGGTGGACAT  
GCTCAGGGAAGCCATCAAGAGGAGAAACGAGTTTGACCTGGACATTGTTGCAGTCGTGAATGATACAG  
TGGGGACCATGATGACCTGTGGCTATGAAGATCCTAATTGTGAGATTGGCCTGATTGCAGGAACAGGC  
AGCAACATGTGCTACATGGAGGACATGAGGAACATCGAGATGGTGGAGGGGGGTGAAGGGAAGATGTG

Appl. No. 10/805,075

PATENT

Amdt. dated January 4, 2005

Reply to Notice to File Missing Parts of June 4, 2004

CATCAATACAGAGTGGGGAGGATTTGGAGACAATGGCTGCATAGATGACATCCGGACCCGATACGACA  
CGGAGGTGGATGAGGGGTCCTTGAATCCTGGCAAGCAGAGATACGAGAAAATGACCAGTGGGATGTAC  
TTGGGGGAGATTGTGCGGCAGATCCTGATCGACCTGACCAAGCAGGGTCTCCTCTTCCGAGGGCAGAT  
TTCAGAGCGTCTCCGGACCAGGGGCATCTTCGAAACCAAGTTCCTGTCCCAGATCGAAAGCGATCGGC  
TGGCCCTTCTCCAGGTGAGGAGGATTCTGCAGCAGCTGGGCCTGGACAGCACGTGTGAGGACAGCATC  
GTGGTGAAGGAGGTGTGCGGAGCCGTGTCCCGGCGGGCGGCCAGCTCTGCGGTGCTGGCCTGGCCGC  
TATAGTGGAAAAAAGGAGAGAAGACCAGGGGCTAGAGCACCTGAGGATCACTGTGGGTGTGGACGGCA  
CCCTGTACAAGCTGCACCCTCACTTTTCTAGAATATTGCAGGAACTGTGAAGGAAGTAGCCCTCGA  
TGTGATGTGACATTCATGCTGTCAGAAGATGGCAGTGGAAAAGGGGCAGCACTGATCACTGCTGTGGC  
CAAGAGGTTACAGCAGGCACAGAAGGAGAACTAG--

Please insert the accompanying paper copy of the Sequence Listing, page numbers 1 to 24, at the end of the application.